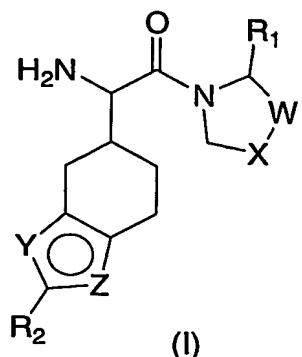


WHAT IS CLAIMED IS:

1. A compound of structural formula I:



5 wherein:

each n is independently 0, 1, 2, or 3;

W is selected from the group consisting of CH₂, CHF, and CF₂;

10 X is selected from the group consisting of S, S(O), S(O)₂, CH₂, CHF, and CF₂;

Y and Z are each independently selected from the group consisting of O, S, N, and NR⁷, with the proviso that at least one of Y and Z is N;

15 R¹ is hydrogen or cyano;

R² is selected from the group consisting of

hydrogen,

halogen,

20 cyano,

hydroxy,

C₁₋₆ alkyl, wherein alkyl is unsubstituted or substituted with one to five halogens,

C₁₋₆ alkoxy, wherein alkoxy is unsubstituted or substituted with one to five halogens,

(CH₂)_n-COOH,

25 (CH₂)_n-COOC₁₋₆ alkyl,

(CH₂)_n-CONR³R⁴,

(CH₂)_n-NR³R⁴,

(CH₂)_n-NR⁶SO₂R⁵,

(CH₂)_n-NR⁶CONR³R⁴,

(CH₂)_n-NR⁶COR⁶,

(CH₂)_n-NR⁶CO₂R⁵,

5 (CH₂)_n-aryl, wherein aryl is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, CO₂H, C₁-6 alkyloxycarbonyl, C₁-6 alkyl, C₃-6 cycloalkyl, and C₁-6 alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens, wherein any methylene (CH₂) carbon atom in R² is independently unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C₁-4 alkyl unsubstituted or substituted with one to five halogens;

10 R³ and R⁴ are independently selected from the group consisting of hydrogen,

15 (CH₂)_n-phenyl,
(CH₂)_n-C₃-6 cycloalkyl, and
C₁-6 alkyl,

20 wherein alkyl is unsubstituted or substituted with one to five halogens and wherein phenyl and cycloalkyl are unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C₁-6 alkyl, and C₁-6 alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens; or

25 R³ and R⁴ together with the nitrogen atom to which they are attached form a heterocyclic ring selected from azetidine, pyrrolidine, piperidine, piperazine, and morpholine wherein said heterocyclic ring is unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, C₁-6 alkyl, and
C₁-6 alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens;

30 each R⁵ is independently selected from the group consisting of (CH₂)_n-phenyl, (CH₂)_n-C₃-6 cycloalkyl, and C₁-6 alkyl, wherein alkyl is unsubstituted or substituted with one to five halogens and wherein phenyl and cycloalkyl are unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C₁-6 alkyl, and C₁-6 alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens, and wherein any methylene (CH₂) carbon atom in R⁵ is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C₁-4 alkyl unsubstituted or substituted with one to five halogens;

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each R⁶ is hydrogen or R⁵; and

R⁷ is selected from the group consisting of

hydrogen,

5 (CH₂)_n-phenyl,

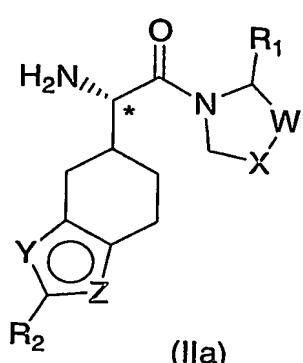
(CH₂)_n-C₃₋₆ cycloalkyl, and

C₁₋₆ alkyl,

wherein alkyl is unsubstituted or substituted with one to five halogens and wherein phenyl and cycloalkyl

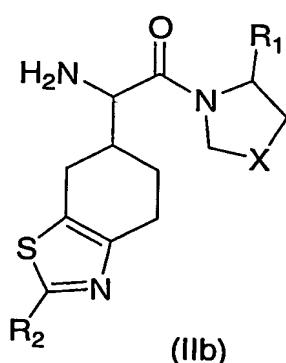
10 are unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens.

2. The compound of Claim 1 wherein the carbon atom marked with an * has the stereochemical configuration as depicted in formula IIa:



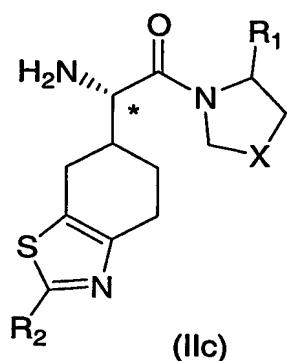
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3. The compound of Claim 1 of structural formula IIb:



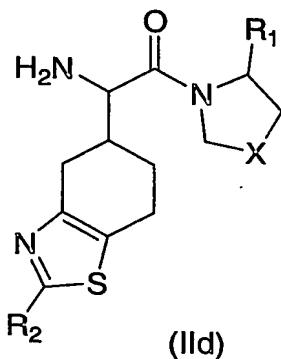
4. The compound of Claim 3 wherein X is CH₂, CHF, or CF₂ and R¹ is hydrogen.

5. The compound of Claim 3 wherein the carbon atom marked with an * has the stereochemical configuration as depicted in formula IIc:



5 and wherein X is CH₂, CHF, or CF₂ and R¹ is hydrogen.

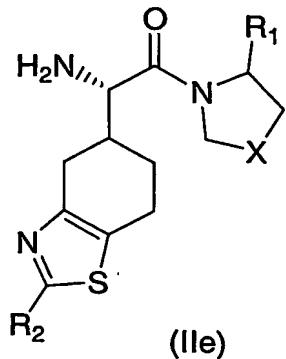
6. The compound of Claim 1 of structural formula Id:



7. The compound of Claim 6 wherein X is CH₂, CHF, or CF₂ and R¹ is hydrogen.

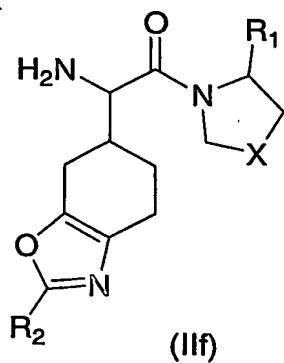
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8. The compound of Claim 6 wherein the carbon atom marked with an * has the stereochemical configuration as depicted in formula IIe:



wherein X is CH₂, CHF, or CF₂ and R¹ is hydrogen.

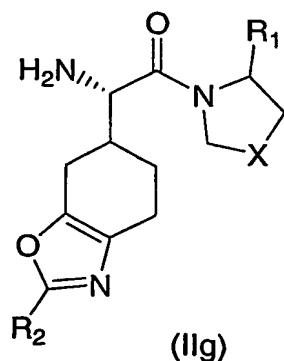
9. The compound of Claim 1 of structural formula IIf:



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10. The compound of Claim 9 wherein X is CH₂, CHF, or CF₂ and R¹ is hydrogen.

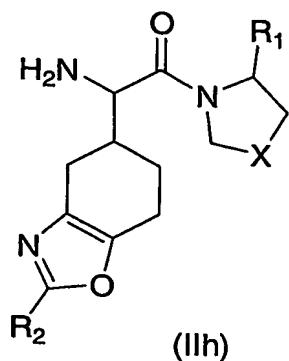
11. The compound of Claim 9 wherein the carbon atom marked with an * has the stereochemical configuration as depicted in formula IIg:



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wherein X is CH₂, CHF, or CF₂ and R¹ is hydrogen.

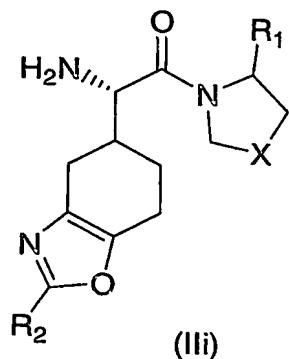
12. The compound of Claim 1 of structural formula IIh:



13. The compound of Claim 12 wherein X is CH₂, CHF, or CF₂ and R¹ is hydrogen.

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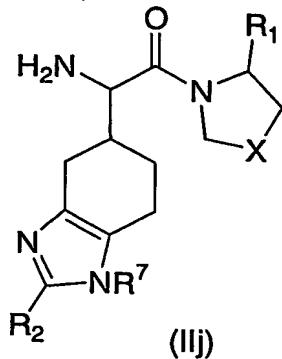
14. The compound of Claim 12 wherein the carbon atom marked with an * has the stereochemical configuration as depicted in formula III:



wherein X is CH₂, CHF, or CF₂ and R¹ is hydrogen.

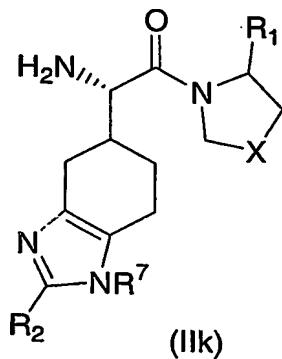
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15. The compound of Claim 1 of structural formula IIj:



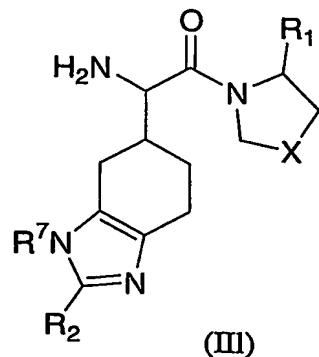
16. The compound of Claim 15 wherein X is CH_2 , CHF , or CF_2 and R^1 is hydrogen.

17. The compound of Claim 15 wherein the carbon atom marked with an * has the stereochemical configuration as depicted in formula IIIk:



wherein X is CH_2 , CHF , or CF_2 and R^1 is hydrogen.

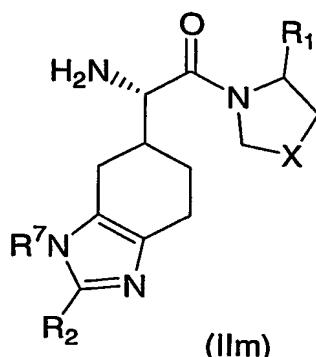
18. The compound of Claim 1 of structural formula III:



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19. The compound of Claim 18 wherein X is CH_2 , CHF , or CF_2 and R^1 is hydrogen.

20. The compound of Claim 18 wherein the carbon atom marked with an * has the stereochemical configuration as depicted in formula II^m:



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wherein X is CH₂, CHF, or CF₂ and R¹ is hydrogen.

21. A pharmaceutical composition which comprises a compound of Claim 1 and a pharmaceutically acceptable carrier.

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22. A method for treating diabetes in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

15 23. A method for treating non-insulin dependent (Type 2) diabetes in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

20 24. A method for treating hyperglycemia in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

25 25. A method for treating obesity in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

26. A method for treating one or more lipid disorders selected from the group of dyslipidemia, hyperlipidemia, hypertriglyceridemia, hypercholesterolemia, low HDL and high LDL in a

mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

27. A method for treating in a mammal in need thereof one or more conditions selected from the group consisting of (1) hyperglycemia, (2) low glucose tolerance, (3) insulin resistance, (4) obesity, (5) lipid disorders, (6) dyslipidemia, (7) hyperlipidemia, (8) hypertriglyceridemia, (9) hypercholesterolemia, (10) low HDL levels, (11) high LDL levels, (12) atherosclerosis and its sequelae, (13) vascular restenosis, (14) irritable bowel syndrome, (15) inflammatory bowel disease, including Crohn's disease and ulcerative colitis, (16) other inflammatory conditions, (17) pancreatitis, (18) abdominal obesity, (19) neurodegenerative disease, (20) retinopathy, (21) nephropathy, (22) neuropathy, (23) Syndrome X, (24) ovarian hyperandrogenism (polycystic ovarian syndrome), and other disorders where insulin resistance is a component, wherein the method comprises the administration to the mammal a therapeutically effective amount of a compound of Claim 1.

15 28. The pharmaceutical composition of Claim 21 further comprising one or more additional active ingredients selected from the group consisting of:

- (a) a second dipeptidyl peptidase IV inhibitor;
- (b) an insulin sensitizer selected from the group consisting of a PPAR γ agonist, a PPAR α/γ dual agonist, a PPAR α agonist, a biguanide, and a protein tyrosine phosphatase-1B inhibitor;

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- (c) an insulin or insulin mimetic;
- (d) a sulfonylurea or other insulin secretagogue;
- (e) an α -glucosidase inhibitor;
- (f) a glucagon receptor antagonist;
- (g) GLP-1, a GLP-1 mimetic, or a GLP-1 receptor agonist;
- (h) GIP, a GIP mimetic, or a GIP receptor agonist;
- (i) PACAP, a PACAP mimetic, or a PACAP receptor agonist;
- (j) a cholesterol lowering agent such as (i) HMG-CoA reductase inhibitor, (ii) sequestrant, (iii) nicotinyl alcohol, nicotinic acid or a salt thereof, (iv) PPAR α agonist, (v) PPAR α/γ dual agonist, (vi) inhibitor of cholesterol absorption, (vii) acyl CoA:cholesterol acyltransferase inhibitor, and (viii) anti-oxidant;
- (k) a PPAR δ agonist;
- (l) an antiobesity compound;
- (m) an ileal bile acid transporter inhibitor;
- (n) an anti-inflammatory agent; and

(o) an antihypertensive agent.

29. The pharmaceutical composition of Claim 28 wherein the PPAR α/γ dual agonist is KRP-297.

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30. A method of treating diabetes in a mammal in need thereof comprising administering to the mammal a therapeutically effective amount of a compound of Claim 1 in combination with the PPAR α/γ dual agonist KRP-297.

10 31. A method of controlling or treating diabetes in a mammal in need thereof comprising administering to the mammal a therapeutically effective amount of a compound of Claim 1 in combination with an insulin sensitizer or an insulin secretagogue.